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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,203	06/29/2006	Simon Michael West	051-167-US	4056

718 7590 12/06/2006

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/551,203	WEST ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/2006*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Information Disclosure Statement filed on September 27, 2005. Claims 1-22 are pending in the application.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claims 1 -22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The words "reaction product' do not explicitly state the nature of the chemical reaction (whether electrovalent or covalent reaction) that takes place between an alkaloid and phosphate derivative of "electron transfer agent". Claim 19 recites "step of reacting alkaloid', but does not recite how it is reached and what product is produced.

Claim 20 provides for the "use" of reaction product of one or more alkaloids with one or more phosphate derivatives of one or more electron transfer agents, together with excipients in the manufacture of a formulation. But, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant

is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Additionally, claims 1-22 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 1-3, 6, 8-22 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Kirby et al. U.S.Patent No. 6,444,234 B1 (herein after '234) in view of WO 02/40033 A1 (herein after '033) or vice-versa.

With respect to claims 1-3, 6, 8-22, ('234) discloses,

Pharmaceutical compositions for the transdermal administration of a medicament or active agent by topical application of the composition to the skin of humans or animals (abstract).

- '(234) Also teaches a method for formulating safe and effective compositions for topical transdermal applications of an active agent such as morphine (column 5 lines 3-5 and col. 42 example 14). The composition as set forth by ('234) comprises an active agent in a "carrier". Said "carrier" comprises solvent and modifying agents. The solvent modifiers facilitate the dissolution of the active agent and formation of the weak association which enable the complex of active agent-modifier to pass the defensive of the skin with minimal irritation without modification of the chemical structure or stereoscopic configuration of the active agent (column 11, lines 5-10). The solvent modifiers selected do not form permanent or strong covalent bonds with the medicament or active agents; instead they form complexes that facilitate the movement of the complex past the viable skin to its targeted site (column 5 lines 53-56).

Although ('234) discloses the use of solvent modifiers in formulating pharmaceutical compositions for the transdermal administration of a medicament or active agent, it does not explicitly teach using phosphate derivatives of tocopherol or other

tocols as claimed in the instant application as solvent modifiers for the same purpose. However, with respect to claims 1 -3, 6,8-20 WO 02/40033 A1 ('033) teaches an efficacious therapeutic emulsion formulation for therapeutic administration comprising phosphate derivatives of "electron transfer agents" and an "acceptable carrier" (abstract).

- According to ('033), the use of a phosphorylated electron transfer agent plays therapeutic and efficacious role in dermal penetration (page 3, lines 3-8).
- The "electron transfer agents" as indicated by ('033), refer to the class of chemicals, which may be phosphorylated. Examples of classes of "electron transfer agents" that may be phosphorylated include hydroxyl chromans including alpha, beta and gamma tocopherol, tocols and tocotrienols in enantiomeric and racemic forms; quinols being the reduced form of vitamin K1 and ubiquinone; hydroxyl carotenoids including retinol and ascorbic acid (page 3, lines 26-28 and page 4, lines 1-2). The phosphate derivatives may exist in the form of a free phosphate acid, a salt thereof, a di-phosphate ester thereby including two molecules of electron transfer agents, a mixed ester including two different compounds selected from electron transfer agents, or a phosphatidyl compound (page 4, lines 5-9).
- ('033) further teaches that the phosphate derivatives of "electron transfer agents" can be combined with 'acceptable carrier". As defined in ('033), the "acceptable carrier" could be classified as drug, food or cosmetics (page 4, lines 30-33 and page 5, lines 1-6). Said "acceptable carrier" can be complexed with

"phosphorylated electron transfer agent" to make parenteral or enteral formulations such as tablets, powders, chewable tablets, capsules, oral suspensions, children formulations, enteral feeds, nutraceuticals and functional foods as claimed in the instant claim 6 (page 5, lines 1-4).

Therefore, based on the afore-described teachings of ('432) and ('033), it would have been prima-facie obvious to one of ordinary skilled in the art at the time of the invention to use the phosphate derivatives of tocopherol ('033) in the compositions of ('234) because ('033) shows that phosphate derivatives of electron transfer agents such as tocopherol phosphate derivatives when complexed with a drug, posses an unexpected property in exhibiting an efficacious role in dermal penetration of the therapeutically active formulation such as topical formulations or formulations such as tablets, powders, chewable tablets, capsules, oral suspensions, children formulations, enteral feeds, or nutraceuticals. Because of the fact that the phosphate derivatives of "electron transfer agents" such as phosphate derivatives of tocopherol or mixtures thereof in combination with an "acceptable carrier" such as drug, food or cosmetic arts exhibit therapeutic properties, one skilled in the art will be motivated to make alkaloid formulations with phosphate derivatives of tocopherol or in other words phosphate derivatives of "electron transfer agent" to bring about efficacious therapeutic effect on dermal penetration with a reasonable expectation of success because ('033) and ('432) both are directed towards the same goal and ('033) provides the guidance. Or alternately to use morphine taught by ('234) in the generic teachings of "drug" in ('033) would have been obvious to one skilled in the art at the time of invention with a reasonable expectation of success since

('033) directed to transdermal delivery and ('234) shows that morphine can be administered transdermally. As such, the claims 1-3, 6, 8-22 of the instant application render themselves rejected based on the afore-mentioned justifications.

5. Claims 4, 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schor et al. (U.S.Patent No. 4,369,172, herein after '172) in view of WO 02/40033 A1 ('033) or vice versa.

The teachings of WO 02/40033 A1 ('033) are disclosed above.

With respect to claims 4, 6-7, Schor et al. teaches,

- Schor et al. ('172) discloses an invention which provides a "carrier material" for use in the preparation of orally, buccally or sublingually administered lozenges and tablets that have a regular and prolonged release pattern for systemically absorbable medicament or active ingredient incorporated therein. Said "carrier material" as defined by Schor et al. is hydroxypropylmethylcellulose (column 2, lines 41-48 and title).
- ('172) teaches that the active ingredient can be of the type of medication which acts locally in the mouth or systemically which in the case of latter can be administered orally to transmit the active medicament into the gastrointestinal tract and into the blood fluids and tissues of the body (column 5, lines 42-50).
- ('172) further discloses that active ingredient can be of the type of medication which acts through the buccal tissues of the mouth to transmit the active ingredient directly into the blood stream.
- ('172) further discloses that morphine can be used as an active ingredient (see

column 6, line 53 and column 2, claim 23).

Schor et al. ('172) does not teach using phosphate derivatives of "electron transfer agents". However, ('033), as discussed above, teaches the complexing of phosphate derivatives of "electron transfer agents" with any generic drug. It would have been obvious to one of ordinary skill in the art at the time, that the invention was made to use phosphate derivatives of tocopherol, or in other words phosphate derivatives of "electron transfer agents" as taught by ('033) to make oral or buccal formulations as taught by Schor et al. because ('033) teaches that phosphate derivatives of "electron transfer agents" such as tocopherol phosphate derivatives, when complexed with a "drug", exhibit enhanced drug absorption and hence, improved drug efficiency of oral formulations such as oral tablets, enteral feeds or oral suspensions.

Because of the fact that the phosphate derivatives of "electron transfer agents" such as phosphate derivatives of tocopherol or mixtures thereof in combination with an "acceptable carrier" such as drug, food or cosmetic exhibit enhanced therapeutic efficiency, one skilled in the art at the time the invention was made would be motivated to make alkaloid formulations with phosphate derivatives of electron transfer agents to bring about efficacious therapeutic effect in oral formulations with a reasonable expectation of success since both ('033) and ('172) are directed towards the same goal and ('033) provides the guidance. Alternately to use any analgesic such as morphine as taught by ('172) in the generic teachings of "drug" as taught by ('033) would have been obvious to one skilled in the art at the time the invention was made with a reasonable expectation of success since ('033) is directed to oral formulations such as

oral tablets or oral suspensions and ('172) shows that a drug such as morphine can be administered orally.

As such, the claims 4, 6-7 of the instant application render themselves rejected based on the aforementioned justifications.

6. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schor et al. (U.S.Patent No. 4,369,172, herein after '172) in view of WO 02/40033 A1 ("033) and further in view of Fisher et al. (US 2004/0234602 A1).

With respect to claim 5,

The teachings of Schor et al. and WO 02/40033 A1 ('033) are discussed above.

Schor et al. do not teach using enteric coatings in the oral formulations disclosed above.

However, Fischer et al. in US publication (U.S. 2004/0234602 A1) discloses a composition with enteric coating and a method for controlling the release of a therapeutically active substance from a pharmaceutical composition into an aqueous medium, wherein the pharmaceutical composition is a coated matrix composition in which the matrix comprises:

a) Polymer or mixture of polymers,
b) An active substance and optionally,
c) One or more excipients
(Page 1, paragraph 1)

- The polymers such as polyethylene oxide or eudragit L methyl ester as disclosed by Fischer et al. (on page 3, paragraph 41 and 43) are an example of enteric coatings. The active substance such as morphine, codeine and atropin can be

used in the above composition (page 4, paragraph 51) in an oral formulation (page 3, paragraph 48). ('172) further teaches that in order to soften the "carrier system", a plasticizer can be selected from group of phosphate esters for e.g. a-tocopherylphosphate esters (page 8 paragraph 100).

Because Fischer et al. teaches that enteral coatings can be used to control release of drug and since it is well known in the art that enteral coatings are used to promote absorption of drugs in the intestine, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to use enteric coatings as taught by Fischer et al. in the teachings advanced by ('172) as modified by ('033). A skilled artisan would be motivated to prepare enteric-coated oral formulations of alkaloids such as morphine or atropine complexed with phosphate derivatives of "electron transfer agents" or in other words phosphate derivatives of tocopherol with reasonable expectations of success because enteric coatings can be used as release modifiers that help in the absorption of the active substance in the intestine. Furthermore, as supported by ('033) by the fact that phosphate derivatives of "electron transfer agents," such as tocopherol phosphate derivatives when complexed with a "drug" possess an improved drug efficiency in the formulations such as enteral feeds, oral tablets or oral suspensions.

Therefore, based on the aforementioned justifications, the claim 5 renders itself rejected.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday-Friday from 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571)-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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